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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/138,735	08/24/98	PARANHOS-BACCALA G	WPB-36400B

HM12/1222

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EXAMINER	
GRASER, J	
ART UNIT	**PAPER NUMBER**
1645	9

DATE MAILED: 12/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/138,735	Paranhos-Baccala et al.
Examiner	**Group Art Unit**
Graser, Jennifer	1645

☒ Responsive to communication(s) filed on *Amendment A, 10/10/00*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 2, and 5-35* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, and 5-35* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted 10/10/2000, Paper No. 8/C is made. Claims 1, 2 and 5-35 are currently pending.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-25 because there is a discrepancy between what is contained on the disk and what is provided in the sequence listing and set forth in the specification. Specifically, , SEQ ID NOS: 8, 9 and 10 contain **AMINO ACID SEQUENCES not** NUCLEIC ACID SEQUENCES. There appears to be a discrepancy in the computer readable form submitted and the sequence listing. Applicants must fix this problem and update the specification accordingly.

APPLICANT IS GIVEN THE SAME TIME PERIOD FOR RESPONDING TO THIS OFFICE ACTION IN ORDER TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the

response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2 and 5-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 5, 8, 17, 20 and 24 are vague and confusing because the beginning of the claim encompasses both RNA and DNA, i.e., "a synthetic or isolated nucleic acid fragment" yet the end of the claims state "or the corresponding RNA sequence". This makes the claims unclear. Further, the claims state that the "synthetic or isolated nucleic acid fragment" may be "fully complementary or antisense"; however, it is unclear how these two sequences would be distinguishable from one another. The phrase appears to be redundant. Appropriate correction is required.

Claims 1, 2 and 5-35 are vague and indefinite due to the use of the term "monomers". When referring to single nucleotides, the use of the term "nucleotide" is preferred as monomer has a different connotation.

Claims 1, 2 and 5-35 currently read on genomic or chromosomal DNA from T.cruzi due to the use of the open language "comprising" which allows much more than the specific segments recited.

Claims 5 and 8 are vague and confusing because it recites that the probe/primer comprises a nucleotide sequence which is "'fully complementary' to at least a segment of five contiguous monomers of a nucleic acid consisting of..." when it appears that Applicants intend for the probe/primer to consist of is "at least five contiguous monomers of a nucleic acid consisting of a sequence which is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at 2207 of SEQ ID NO:1 or the corresponding RNA sequence.". The use of fully complementary in two different places leaves the claim vague and confusing and becomes unclear which sequence is actually being claimed. A sequence which is at least a five contiguous segment monomer which is "fully complementary" to a sequence which is "identical to SEQ ID NO:1" and to a sequence which "is fully complementary to SEQ ID NO:1" leaves the claim very confusing and unclear. Appropriate correction is required.

Claim 10 is vague and indefinite because it recites a primer according to claim 9 which consists of nucleotide sequences selected from the group consisting of SEQ ID NO: 8, 9, 10 and 12. However, SEQ ID NOS: 8, 9 and 10 contain **AMINO ACID SEQUENCES not** NUCLEIC ACID SEQUENCES. There appears to be a discrepancy in the computer readable form submitted and the sequence listing. Applicants must fix this problem. Appropriate correction is requested. SEE SEQUENCE COMPLIANCE RULES below.

Claims 21, 22 and 23 vague and indefinite because it is unclear what is meant by *"any succession'* of 30 contiguous monomers". Clarification is requested.

Claims 25 and 26 are vague and confusing because it is unclear which "nucleotide sequence" this claim is referring to, i.e., the one the probe comprises or the one that the probe is fully complementary.

Claim 27 is vague and indefinite because it fails to state the hybridization conditions. A process which utilizes low stringency conditions would not accurately detect T.cruzi but instead would detect many unrelated organisms as well.

It is requested that Applicant use more straightforward language to convey their invention. The use of double negatives....i.e., something which is fully complementary to something which is fully complementary or identical or antisense is extremely confusing and does not allow for one to readily identify what is actually being claimed. The exact nucleotides being claimed should be set forth and the methods of using them. The coverage afforded would be the same and would not lead to such inherent confusion.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2 and 5-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced or its ability to function as a probe or primer. Further, it is unpredictable as to which nucleotides could be removed and which could be added. Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than 85% a variance as up to 70-95% or more from SEQ ID NO:1. It is unclear what sequence this encompasses and what function it would serve. The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the probe or primer to be produced. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable

nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112- Written description

7. Claims 1, 2 and 5-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:1, SEQ ID NO: 1 (1232-1825), SEQ ID NO:1 (1232-2207) and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to sequences which are 85% homologous to a 30 nucleotide segment and fragments which contain sequences which are complementary to sequences which are antisense which are 5 and 8 nucleotides in length, etc..

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a

precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for antisense and sequences and fragments of varying percent identity is stated. However, no disclosure, beyond the mere mention of these potential sequences is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of nucleotides 1232-1825, 1232-2207 of SEQ ID NO:1 or SEQ ID NO:1 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. Claims 5, 6, 8, 9, 10, 25, 28 29, 30, and 32 are rejected under 35 USC 102(b)/(a) as being anticipated by any one of Ko et al (Gencore Accession # M30933, 1990) and Opperman et al (Gencore Accession # L27277 from J.Bacteriol. 1994. 176(16): 5033-5043)..

Ko et al. and Opperman et al. both disclose a sequence which comprises at least 5 contiguous nucleotides of SEQ ID NO: 1, nucleotides 1232 and 1825 and nucleotides 1232-2207 of SEQ ID NO: 1. Ko teaches a segment which comprises 7 contiguous nucleotides of SEQ ID NO: 1, nucleotides 1232 and 1825. The attached sequence alignment mailed with the previous Office Action is a database search of nucleotides 1232-1825 of SEQID NO: 1 which are referred to as nucleotides 1-594 on the alignment. One can see several contiguous pieces of 5 monomers which correspond to SEQ ID NO:1 and which are no more than 100 nucleotides.

Response to Applicants' Arguments:

Applicants have argued that the amendments have overcome this rejection. This has been fully and carefully considered but is not deemed persuasive for the reasons set forth above.

Claim Rejections - 35 USC § 102

10. Claims 5, 6, 7, 8, 9, 10, 11, 17, 25, 26, 2829, 30, 31, 32, and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by any one of Barton (Genbank Accession No: T07199 corresponding to US Patent No. 5,474,925) or John (Genbank Accession No. T13034 corresponding to US Patent No. 5,495,070).

Barton and John both disclose a nucleotide sequence which comprises at least 8 contiguous nucleotides of SEQ ID NO: 1, nucleotides 1232 and 1825 and nucleotides 1232-2207

of SEQ ID NO: 1. The attached sequence alignment is a database search of nucleotides 1232-1825 of SEQ ID NO: 1 which are referred to as nucleotides 1-594 on the alignment.

Information Disclosure Statement

11. Applicants stated that they filed a PTO-1449 on 8/24/98. This PTO-1449 is not of record in the case and has not been received by the Examiner. Applicants should re-submit the PTO-1449 and the references which are cited on it in order to make it of record.

11. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jennifer Graser
Primary Examiner 12/20/00
Art Unit 1645